STERIC EFFECTS IN REACTIONS OF ORGANOLITHIUM COMPOUNDS

By

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Chapter I

INTRODUCTION

A. Statement of Problem

The primary purpose of this investigation has been to determine the nature of the interplay among the steric factors which influence the ratio of products obtained in the reaction of o-substituted phenyllithium compounds with o-substituted phenyl and o-cresyl benzoates. The products of these reactions are the corresponding o-substituted benzophenones and triphenylcarbinols. Alkyl groups of various sizes were employed as substituents in three specific areas: the acyl portion of the ester, the alcohol portion of the ester, and the phenyllithium reagent. Also, from a comparison of the yields of carbinols obtained in this reaction with those derived from the reaction of the phenyllithium reagents with o,o'-disubstituted benzophenones and p-cresyl benzoates, it was hoped that a mechanism consistent with the data could be suggested. Finally, by deriving a series of kinetic equations for the proposed mechanism steps and calculating the resulting relative rate factors, it was desired to determine a quantitative relationship between the size of the substituent and its effect upon the course of the reaction.

B. Historical

The first mention of any steric effects in the reactions of

organolithium compounds appeared in an article by Gilman and Kirby (1). They investigated the difference in reactivity of phenyllithium and phenylmagnesium bromide with N-diphenylmethyleneaniline (benzophenone anil). The failure of the Grignard reagent to add across the carbon-nitrogen double bond, in contrast to the excellent yield of triphenylmethylaniline obtained with phenyllithium, was attributed not only to the relative sizes of the organometallic compounds but also to the steric effects of the accumulated phenyl substituents.

Similarly, numerous instances have been reported where organolithium reagents gave good yields of tertiary alcohols from reaction with ketones and esters, while the corresponding Grignard reagents gave little or none of the desired product (2-20). The greater reactivity of the organolithium compounds is undoubtedly a significant factor in these cases, but the steric effects present in both the organometallic reagents and the substrates must certainly contribute to this reactivity. For example, yields of over 90 per cent of dimethylisopropylcarbinol were reported in the reaction of ethyl isobutyrate with methylmagnesium bromide (21), while no tertiary alcohol was obtained in the reaction of t-butylmagnesium bromide with the ester (22). t-Butyllithium gave 66 per cent of di-t-butylisopropylcarbinol with the same ester (20).

The carbonation of a series of hindered phenyllithium compounds has been reported (12), and the results were interpreted in light of the steric effects of the substituent alkyl groups. These results are given in Table 1.

Two methods of carbonation were studied in which the ratio of carbon dioxide gas to organolithium reagent was reversed. Method A

TABLE 1

CARBONATION OF PHENYLLITHIUM COMPOUNDS (12)

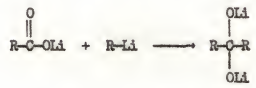
Phenyllithium Compound	Temp. °C	Method	Yield of Acid (per cent)	Yield of Other Product (per cent)
Phenyllithium	25	A	0	58 – benzophenone
	0	B	72	8 – triphenylcarbinol
o-Methyl-	25	A	30	
	0	B	69	
2,4,6-Triisopropyl-[a]	25	A	53[b]	
	0	B	87[b]	
2,3,5,6-Tetraisopropyl-[a]	17	A	52[b]	
2,5-Di-t-butyl-[a]	17	A	53[b]	

a. Obtained by halogen-metal interconversion from aryl bromide and n-butyllithium.

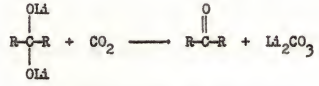
b. Based on aryl bromide.

consisted of passing a stream of the dry gas over an ether solution of the organolithium compound, and in method B a stream of the ether solution was introduced through a nozzle into an atmosphere of the dry gas. The equations for the reaction can be represented by

Eq. 1



Eq. 2



Eq. 3

Only ketone, resulting from the hydrolysis of the reaction product from equation 2, was isolated from the carbonation of phenyllithium by method A; not enough carbon dioxide was present for the third reaction to occur. With excess carbon dioxide however the acid was obtained, and the ketone formed from the third reaction was responsible for the production of triphenylcarbinol. As steric hindrance increased the second reaction did not occur, and good yields of acid were obtained by either method.

Faber and Nauta (4) prepared a series of symetrically substituted methyltriphenylcarbinols by the reaction of methyl substituted phenyllithium reagents with the appropriate ketone. In this way they were able to report the synthesis of the tertiary alcohols listed in Table 2 in the indicated yields. It is interesting to note that

TABLE 2

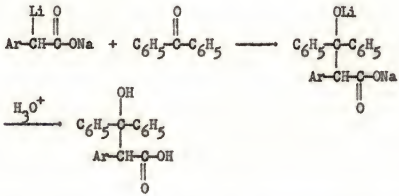
YIELDS OF TRIPHENYLCARBINOLS FROM REACTIONS OF SUBSTITUTED PHENYLLITHIUM COMPOUNDS WITH SUBSTITUTED BENZOPHENONES (4)

Phenyllithium Compound	Benzophenone	Yield of Product (per cent)
o-Methyl-	Di-o-methyl-	47
m-Methyl	Di-m-methyl-	23
p-Methyl-	Di-p-methyl-	66
2,3-Dimethyl-	2,2',3,3'-Tetramethyl-	35
2,4-Dimethyl	2,2',4,4'-Tetramethyl-	59
2,5-Dimethyl-	2,2',5,5'-Tetramethyl-	24
3,5-Dimethyl-	3,3',5,5'-Tetramethyl-	18

substitution in the 3-position seemed to exert the greatest steric interference.

In a steric study of the action of bornyllithium or hindered ketones, it was found that only in extremely hindered cases the expected tertiary alcohol was not formed (12). Di-t-butylbornylcarbinol and t-butylphenylbornylcarbinol were produced in 40 to 60 per cent yields respectively. 3-Amino-2,4,6-triisopropylbenzophenone and 3-ethylamino-2,4,6-triisopropylbenzophenone gave little or no reaction with bornyllithium. No products were isolated in these latter reactions.

An investigation of the reactions of organolithium compounds obtained by substitution of labile hydrogen atoms has also been reported (23, 24, 25). In one series, α-lithio derivitives of the sodium salts of phenylacetic acid, α-naphthylacetic acid, and β-naphthylacetic acid were reacted with benzophenone to give substituted β-hydroxypropionic acids. The preparation of the α-lithio compounds was accomplished through reaction of various alkyllithium reagents with the acid salts. The equations for the reactions are given by



The yields of acids obtained from the organolithium compounds are listed in Table 3.

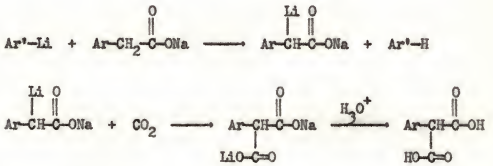
TABLE 3

YIELDS OF ACIDS OBTAINED FROM THE REACTION OF ALKYLLITHIUM COMPOUNDS, SODIUM ARLYACETATES, AND BENZOPHENONE (23, 24, 25)

Alkyllithium Compound	Acid Salt	Yield of Acid (per cent)
Propyl-	Sodium phenylacetate	45
Isopropyl-	Sodium phenylacetate	23
n-Butyl-	Sodium phenylacetate	47
Isobutyl-	Sodium Phenylacetate	35
s-Butyl-	Sodium phenylacetate	18
t-Butyl-	Sodium phenylacetate	12
Propyl-	Sodium α-naphthylacetate	45
Isopropyl-	Sodium α-naphthylacetate	15
n-Butyl-	Sodium α-naphthylacetate	41
Isobutyl-	Sodium α-naphthylacetate	10
Propyl-	Sodium β-naphthylacetate	37
Isopropyl-	Sodium β-naphthylacetate	8
n-Butyl-	Sodium β-naphthylacetate	32
Isobutyl-	Sodium β-naphthylacetate	27

Since a benzophenone solution was added to the reaction mixture of the alkyllithium reagent and the acid salt, the results show the ability of the organolithium compounds to metallate the acid salts. It is evident that as chain branching increased this ability decreased. In the second reaction the α-lithio derivitives of sodium phenylacetate and sodium α-naphthylacetate were able to add more readily to benzophenone than was the α-lithio derivitive of sodium β-naphthylacetate.

The results of a parallel study (23, 26, 27) in which substituted phenyllithium compounds were employed to metallate acid salts and the product carbonated are summarized in Table 4. The equations for the reactions are as follows:



The generally lower yields of di-acids obtained with the less hindered aryllithium compounds and sodium β-naphthylacetate were attributed to the following side reaction.

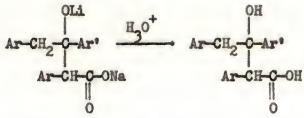
TABLE 4

YIELDS OF DIACIDS OBTAINED BY CARBONATION OF SODIUM α-LITHIOARYLACETATES (23, 26, 27)

Aryllithium Compound	Acid Salt	Yield of Diacid (per cent)
Phenyl-	Sodium α-naphthylacetate	38[a]
o-Methylphenyl-	Sodium α-naphthylacetate	48
m-Methylphenyl-	Sodium α-naphthylacetate	35
p-Methylphenyl-	Sodium α-naphthylacetate	19
α-Naphthyl-	Sodium α-naphthylacetate	37
Phenyl-	Sodium β-naphthylacetate	19[b]
o-Methylphenyl-	Sodium β-naphthylacetate	42
m-Methylphenyl-	Sodium β-naphthylacetate	19
p-Methylphenyl-	Sodium β-naphthylacetate	22
α-Naphthyl-	Sodium β-naphthylacetate	26

a. A 12 per cent yield of the ketone also isolated.

b. A 27 per cent yield of the ketone also isolated.



When steric hindrance was increased, the amount of side reaction was reduced, as is evidenced by the higher yields of di-acids in the sodium α-naphthylacetate series and in the reactions of α-naphthyllithium and o-methylphenyllithium.

The findings of a steric study (28) of this side reaction are found in Table 5. These unhindered aryllithium reagents gave both benzyl aryl ketones and substituted β-hydroxybutyric acids, but o-methylphenyllithium, mesityllithium, and α-naphthyllithium yielded only sodium α-lithio-phenylacetate. Steric effects evidently prohibited any further reaction.

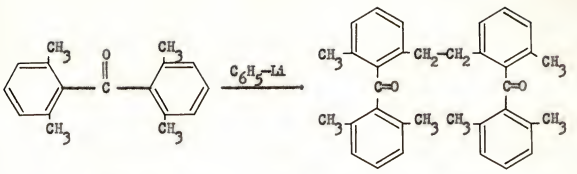
The reaction of organolithium compounds with highly hindered ketones and some α,β-unsaturated ketones may lead to abnormal addition products. It has been shown (4, 29, 30) that tetra-o-methyl substituted benzophenones react with aryllithium compounds in such a manner that the latter do not add across the carbonyl group, but involve the o-methyl substituent. The same product was obtained in the reactions of phenyllithium and mesityllithium with 2,2',6,6'-tetramethylbenzophenone.

The overall reaction can be represented by

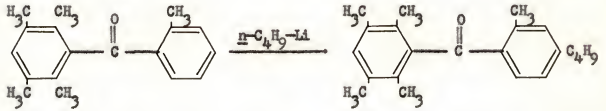
TABLE 5

YIELDS OF BENZYL ARYL KETONES AND SUBSTITUTED
β-HYDROXYBUTYRIC ACIDS OBTAINED FROM REACTIONS OF
ARYLLITHIUM COMPOUNDS WITH SODIUM PHENYLACETATE (28)

Aryllithium Compound	Acid Salt	Yield of Acid (per cent)	Yield of Ketone (per cent)
Phenyl-	Sodium phenylacetate	41	18
p-Methylphenyl-	Sodium phenylacetate	44	25
m-Methylphenyl-	Sodium phenylacetate	40	32
β-Naphthyl-	Sodium phenylacetate	53	—

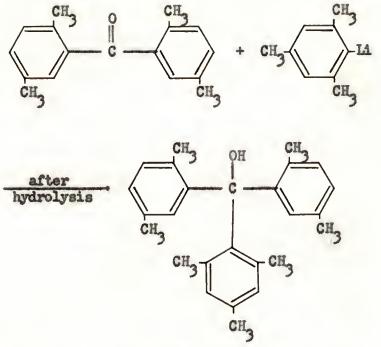


A 17 per cent yield of o-duroylphenylacetic acid obtained from carbonation of the reaction mixture between n-butyllithium and duryl o-methylphenyl ketone (31) confirmed the above observation. However, from a neutral fraction of this reaction a product subsequently identified as duryl 2-methyl-4-butylphenyl ketone was obtained in a 40 per cent yield (32). This was the first report of 1,6-addition by an organolithium reagent.

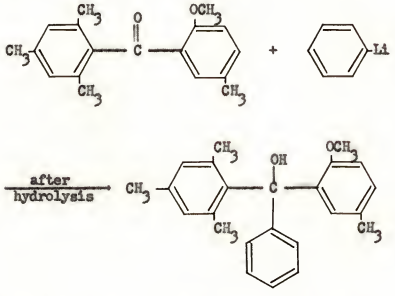


No evidence was obtained as to the nature of the presumed dihydro intermediate or as to the manner by which the aromatic character of the ring was restored. Duryl phenyl ketone also gave predominately 1,6-addition in reaction with n-butyllithium (32).

Diphenyldurylcarbinol and diphenylmesitylcarbinol were prepared in good yields (60-70 per cent) by reaction of duryllithium and mesityllithium with benzophenone (33). 2,2',5,5'-Tetramethyldiphenylmesitylcarbinol was also prepared in a 30 per cent yield from mesityllithium and the appropriate ketone (33)

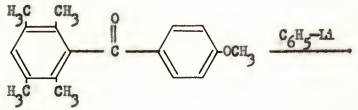


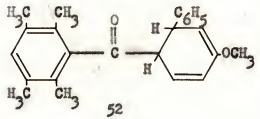
and 2-methoxy-5-methylphenylmesitylphenylcarbinol resulted from the following reaction in a 57 per cent yield.



These good yields of tertiary alcohols from such highly hindered systems were not always readily obtainable. The following dihydro compounds resulting from 1,4-addition of the organolithium

reagent to the hindered ketone were obtained in the indicated per cent yields (33).





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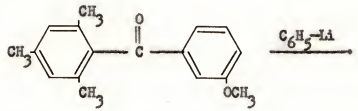

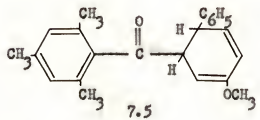

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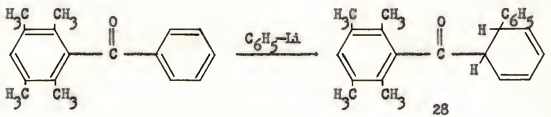

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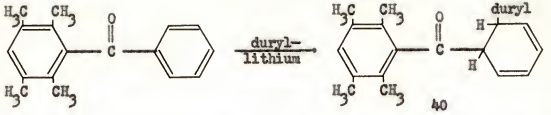

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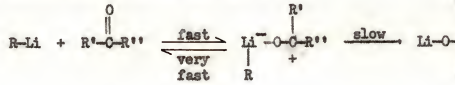
9–Fluorenyllithium was reported to undergo 1,4–addition to a series of α,β–unsaturated ketones (34), and in a study of the reaction of phenylmetallic compounds with benzalacetophenone it was shown that those of intermediate activity, as phenyllithium, gave both 1,2– and 1,4–addition with a preference for the former (35).

The addition of organolithium compounds to ketones has been investigated in detail (36), and a mechanism consistent with the observed second order kinetics proposed.



This mechanism involved a rapid reversible formation of a complex between the lithium reagent and the oxygen atom of the ketone, followed by a rate determining rearrangement of this complex. The order of the reactivity of different lithium compounds was characteristically that of ionic, or Wagner–Meerwein type of rearrangements. Retention of configuration in the R group during migration has also been shown to occur in the reaction of cis– and trans– propenyllithium with various ketones (37).

In a comparison of the reactions of sodium, lithium, and potassium phenylacetylenes with acid derivitives (38) it was found that the sodium reagent yielded primarily ketone, the lithium reagent gave

predominately tertiary alcohol, and the potassium compound reacted less readily, if at all.

The reaction of isopropyllithium with a series of esters of aliphatic mono- and dicarboxylic acids afforded good yields of tertiary alcohols along with some ketones (18). In the case of diethyl malonate, cleavage products were obtained which paralled the reported cleavage of β-diketones by phenyllithium (39).

The reaction of the methyl esters of perfluoroacetic acid, perfluoropropionic acid, and perfluoro-n-butyric acid with phenyllithium in a 1:1 mole ration gave 20-75 per cent tertiary alcohol formation (40). Well over 90 per cent of the lithium reagent reacted, and a corresponding amount of ketone was formed.

t-Butyllithium was observed to react normally with esters, unlike the corresponding Grignard reagent, and gave yields of the expected ketone and tertiary alcohol (20). The results of this study are summarized in Table 6.

From these considerations it appears that organolithium compounds are excellent reagents for the preparation of tertiary alcohols from esters and ketones, even in considerably hindered systems. Their high reactivity and selectivity in adding to the carbonyl group provide for a minimum of side reactions. Only in extremely hindered cases or in reaction with tailor-made α,β-unsaturated ketones are any abnormal reaction observed.

TABLE 6

YIELDS OF TERTIARY ALCOHOLS AND KETONES FROM REACTIONS OF *t*-BUTYLLITHIUM WITH ESTERS (20)

Ester	Yield of Alcohol (per cent)	Yield of Ketone (per cent)
Methyl formate	85	—
Methyl acetate	80	6
Methyl propionate	79	7
Methyl isopropionate	88	1
Methyl butyrate	67	11
Methyl pentanoate	64	14
Methyl hexanoate	60	23
Methyl heptanoate	50	30

Chapter II

EXPERIMENTAL

A. General Procedures

The organolithium compounds from bromo-, o-methylbromo-, o-ethylbromo-, and o-isopropylbromobenzene were reacted with the phenyl and o-cresyl esters of benzoic, o-methylbenzoic, p-methylbenzoic, o-ethylbenzoic, and mesitoic acid. o-Methylphenyllithium and o-ethylphenyllithium were also reacted with the p-cresyl esters of benzoic and o-methylbenzoic acid. Finally, the lithium reagents were allowed to react with benzophenone, o,o'-dimethylbenzophenone, and o,o'-diethylbenzophenone.

The Grignard reagents from the alkylbromobenzenes were carbonated to give the corresponding acids. These acids were converted to the acid chlorides and reacted with the phenols to give the desired esters. The ketones were prepared by the reaction of the appropriate Grignard reagent with the acid chloride.

The phenyllithium compounds were prepared from the corresponding alkylbromobenzenes and lithium metal in diethyl ether. Analyzed solutions of the reagents were reacted in a 1:1 mole ratio with an ether solution of the ester or ketone. The reactions were run at room temperature for one hour. After working up the product the ether was replaced by toluene, and the concentrations of tertiary alcohol, ketone, and unreacted ester were determined by infrared absorption spectrophotometry.

A number of tertiary alcohols resulting from the reactions of phenyllithium compounds with the ketones were isolated and compared with those obtained from the reactions of the phenyllithium reagents with the esters.

All temperatures reported in this work are uncorrected, and microanalyses were performed by Galbraith Laboratories, Knoxville, Tennessee.

B. Starting Materials

Alkylbromobenzenes

Bromobenzene and o-methylbromobenzene were obtained from Dow Chemical Company, and o-ethylbromobenzene was purchased from Aldrich Chemical Company. o-Isopropylbromobenzene was prepared from o-bromobenzoic acid in a three step synthesis, and bromomesitylene was prepared according to the procedure of Smith (41).

Esterification of o-bromobenzoic acid. Five hundred grams (2.5 moles) of o-bromobenzoic acid (Eastman Kodak, m.p. 149-150° C after recrystallization from aqueous ethanol), 1.5 liters of absolute ethanol, and 50 grams of concentrated sulfuric acid were refluxed for fifteen hours in a 3-liter flask. The excess ethanol was distilled from the product, and the residue poured into 2 liters of cold water. This mixture was then extracted with 1.5 liters of ether in three equal portions, the extracts combined, and the ether evaporated on a warm water bath under the reduced pressure of a water aspirator. The ester was dried over anhydrous magnesium sulfate and distilled through a one-foot Vigreux column. The boiling point of the ethyl o-bromobenzoate was 135-136° C, and the yield was 95 per cent.

Preparation of o-bromophenyldimethylcarbinol. In a 3-liter three-necked flask fitted with a true bore stirrer, dropping funnel, and condenser with an outlet for the entrance of dry nitrogen were placed 73 grams (3.0 gram atoms) of magnesium turnings and 1 liter of sodium-dried ether. The system was swept with dry nitrogen and a nitrogen atmosphere was maintained over the system throughout the reaction (42). To this was added 426 grams (3.0 moles) of methyl iodide over a period of two hours. After the addition, the mixture was refluxed for thirty minutes. A solution of 265 grams (1.16 moles) of ethyl o-bromobenzoate in 500 mol. of dry ether was then added over a period of one hour, and the mixture refluxed for an additional two hours. The resulting solution was poured into 500 ml. of ice water, in which had been dissolved 250 grams of ammonium chloride. The ether layer was separated, and the aqueous layer extracted twice with 200-ml. portions of ether. The organic layers were combined and the ether removed as before. The dark product was dried over anhydrous magnesium sulfate and fractionated through a one-foot Vigreux column. The average yield of two runs was 86 per cent. The boiling point of the o-bromophenyldimethylcarbinol was 90-91° C at 1mm.; the reported value is 87-93° C at 1mm. (43).

Preparation of o-isopropylbromobenzene. The reduction of the carbinol was carried out according to the method of Bradshaw (44). One hundred and five grams (0.49 mole) of o-bromophenyldimethylcarbinol, 23 grams of iodine, and 23 grams of red phosphorus were added to 1 liter of acetic acid and 100 ml. of water. After the mixture was refluxed for twenty-four hours the phosphorus was removed by filtration through a large Buchner funnel fitted with an asbestos mat. The

filtrate was cooled, neutralized by addition of solid sodium hydroxide, and extracted with two 200-ml. portions of ether. The combined extracts were washed with 150 ml. of a 10 per cent sodium hydroxide solution and the ether removed as before. The combined products of four runs were dried over anhydrous magnesium sulfate and distilled through a one-foot Vigreux column. The fraction boiling from 103-109° C at 20mm. was collected. The overall yield was 73 per cent.

Preparation of bromomesitylene. In a 2-liter three-necked flask provided with a mechanical stirrer, dropping funnel, and a side arm equipped with a reflux condenser and thermometer was placed 318 grams (2.65 moles) of mesitylene (redistilled, b.p. 163-165° C) dissolved in 200 ml. of carbon tetrachloride. A rubber tube leading from the top of the condenser to a drain served to remove the hydrogen bromide vapors. The flask was cooled to 5° C with an ice bath, and a solution of 450 grams (2.8 moles) of bromine in 280 ml. of carbon tetrachloride was added over a period of three hours maintaining the temperature below 10° C. After the addition was complete, the mixture was refluxed for one hour. The solution was washed with two 300-ml. portions of water and two 250-ml. portions of a 10 per cent sodium hydroxide solution. The reaction mixture was then dried over calcium chloride and the solvent distilled through a one-foot Vigreux column. The residue was added to a solution of 25 grams of sodium in 500 ml. of 95 per cent ethanol and refluxed for one hour. After standing overnight the mixture was diluted with 3 liters of water and separated. The water layer was extracted with three 150-ml. portions of carbon tetrachloride which were added to the crude product, and dried over calcium chloride. The solvent was distilled through a one-foot Vigreux column. After all the

solvent was removed the product was fractionated through this same column under reduced pressure. The fraction of bromomesitylene boiling at 104–107° C at 16mm. was collected in a yield of 72 per cent.

Each of the o-alkylbromobenzenes was further purified by fractionation through a heated, two-foot Podbielniak column equipped with a variable take-off head. Essentially the same procedure was employed in each distillation. The column was allowed to attain equilibrium at infinite reflux for at least two hours. A first fraction representing from 10 to 15 per cent of the starting material was discarded, and a middle cut with a maximum boiling range of 1° C was collected at a reflux ratio of approximately 20:1. The observed physical properties of these reagents along with the literature values are listed in Table 7.

Alkylbenzoyl chlorides

Reagent Grade benzoyl chloride was employed without further purification. The acids synthesized from the carbonation of the Grignard reagents (46) of o-methylbromobenzene, o-ethylbromobenzene, and bromomesitylene were converted to the acid chlorides by reaction with thionyl chloride (47). p-Methylbenzoyl chloride was prepared from p-methylbenzoic acid (Matheson, Coleman and Bell, m.p. 179–181° C) and this same reagent. The same procedure was employed throughout and only one example will be given.

Preparation of o-methylbenzoyl chloride. A 2-liter three-necked flask fitted with a magnetic stirrer, dropping funnel, and a condenser equipped for the entrance of a gas was swept with dry nitrogen for thirty minutes. To the flask was added 37 grams (1.5 gram atoms) of magnesium and enough of a 1-liter portion of sodium-dried ether to cover the turnings. Twenty grams of a 256-gram (1.5 moles) portion of

TABLE 7

PHYSICAL CONSTANTS OF THE PURIFIED ALKYLBROMOBENZENES

Alkylbromobenzene	Index of Refraction, 20° C		Boiling Point, °C, 20mm.	
	Observed	Literature (45)	Observed	Literature (45)
Bromobenzene	1.5595	1.5597	61.5	61.7
o-Methylbromobenzene	1.5563	1.5566	82.0	82.3
o-Ethylbromobenzene	1.5490	1.5487	97.0-97.5	97.6
o-Isopropylbromobenzene	1.5404	1.5408	106-107	107.1
Bromomesitylene	1.5524	—	107-108[a]	105-107[a,b]

a. Boiling point at 16mm.

b. From reference (41).

o-methylbromobenzene was introduced and the reaction initiated by the addition of a few milliliters of a test tube scale Grignard preparation of methylmagnesium iodide. The rest of the o-methylbromobenzene dissolved in the remaining ether was added over a period of one hour. The reaction was exothermic and maintained a gentle reflux during the addition. After the reagent was added the reflux was continued for one hour, and the reaction mixture was cooled and poured in a fine stream into a Dry Ice-ether mixture. After attaining room temperature the liquid was poured onto 1 kg. of cracked ice to which had been added 185 ml. of concentrated hydrochloric acid. When all the ice had melted the ether layer was separated and extracted with 1 liter of 10 per cent sodium hydroxide in four equal parts. Acidification of the basic solution with concentrated hydrochloric acid precipitated the o-methylbenzoic acid. It was collected on a Buchner funnel, air dried, and used without further purification. The yield was 86 per cent. One hundred and seventy-four grams (1.3 moles) of o-methylbenzoic acid was refluxed for eight hours with 250 grams (1.75 moles) of thionyl chloride in a 500-ml. flask equipped with an ice-water condenser. After this time gas evolution ceased, and the solution was dark yellow. The condenser was replaced with a Claisen head fitted with a Friedrich condenser, and the excess thionyl chloride removed under the reduced pressure of a water aspirator. When the pot temperature reached 90° C the system was connected to a vacuum pump and the product distilled. After discarding a small forerun the o-methylbenzoyl chloride was collected at 112-113° C at 30mm. The yield was 77 per cent.

Preparation of p-methylbenzoyl chloride. One hundred grams (0.74 mole) of p-methylbenzoic acid gave an 80 per cent yield of the acid chloride; the boiling point was 89.0-89.5° C at 8mm.

Preparation of o-ethylbenzoyl chloride. One hundred and forty-eight grams (0.8 mole) of o-ethylbromobenzene gave a 91 per cent yield of o-ethylbenzoic acid which in turn gave an 84 per cent yield of the acid chloride when treated with thionyl chloride in the above manner. The boiling point was 121-122° C at 30mm.

Preparation of mesitoyl chloride. Carbonation of the Grignard reagent from 160 grams (0.8 mole) of bromomesitylene gave 68 per cent yield of mesitoic acid. The acid was converted to mesitoyl chloride, boiling point 116.5-118° C at 19mm., in a 92 per cent yield.

Phenyl benzoates

The esters were prepared according to the method of Hickenbottom (48). Phenol (Merck Reagent Grade), o-cresol (redistilled, b.p. 98-99° C at 30mm.), and p-cresol (redistilled, b.p. 128-129° C at 40mm.) dissolved in anhydrous pyridine (Merck Reagent Grade) were reacted with the appropriate acid chlorides. The solid esters were recrystallized from methanol, and those which were liquids were distilled through a small fractionating column. A sample preparation is given below, and the yields and physical constants of the prepared esters are listed in Table 8.

Preparation of phenyl o-methylbenzoate. Twenty-eight grams (0.3 mole) of phenol was dissolved in 150 ml. of dry pyridine in a 500-ml. Erlenmeyer flask which had previously been cooled to 5° C in an ice bath. The flask was stoppered and recooled in the ice bath. When the temperature again reached 5° C, 46 grams (0.3 mole) of o-methylbenzoyl chloride was quickly added with vigorous shaking. The stopper was replaced and the reaction mixture allowed to stand at room temperature overnight. The resulting paste was then poured into a mixture of 50

TABLE 8

YIELDS AND PHYSICAL CONSTANTS OF THE PREPARED ESTERS

Ester	Yield (per cent)	Boiling Point °C	Melting Point °C
Phenyl benzoate	95		70.5–71
o-Cresyl benzoate	89	106–107/0.2mm.	
p-Cresyl benzoate	87		71–72
Phenyl o-methylbenzoate	86	105–106/0.1mm.	
o-Cresyl o-methylbenzoate	90	117.5–119/0.4mm.	
p-Cresyl o-methylbenzoate	92	112–114/0.2mm.	
Phenyl p-methylbenzoate	82		76–76.5
o-Cresyl p-methylbenzoate	78		48.5–49
Phenyl o-ethylbenzoate	75	119–120.5/0.6mm.	
o-Cresyl o-ethylbenzoate	84	125–127/0.6mm.	
Phenyl mesitoate	63		37.5–38
o-Cresyl mesitoate	58		68.5–69

grams of ice and 100 ml. of a 1.5 per cent solution of hydrochloric acid. When the ice had melted 250 ml. of ether was added and the organic layer separated. The ether solution was washed four times with an equal volume of a 1.5 per cent hydrochloric acid solution, three times with an equal volume of a 3 per cent sodium carbonate solution, twice with an equal volume of a 2 per cent solution of sodium hydroxide, and finally, four times with distilled water. Extra solvent was added when necessary. The ether layer was dried by filtering twice through a funnel containing anhydrous sodium sulfate. The solvent was removed with the aid of a warm water bath and the reduced pressure of a water aspirator. A six-inch tube filled with calcium chloride was inserted between the flask and the aspirator. The residue was then placed in a 100-ml. flask and distilled through a six-inch Vigreux column wrapped with glass wool insulation. The condenser was connected to a "cow" with four receivers so the various fractions could be collected without interrupting the distillation. In this way 52 grams (72 per cent) of phenyl o-methylbenzoate, boiling at 105-106° C at 0.1mm., was collected.

The prepared o-cresyl mesitoate has not previously been reported and a sample was submitted for analysis.

Anal. Calcd. for $C_{17}H_{18}O_2$: C, 80.28; H, 7.14. Found: C, 80.22; H, 7.17.

Alkylbenzophenones

Reagent Grade benzophenone was recrystallized from petroleum ether (b.p. 40-60° C) and melted at 47.5-48° C. o,o'-Dimethylbenzophenone and o,o'-diethylbenzophenone were synthesized utilizing the method of Whitmore and Badertscher (49).

Preparation of o,o'-dimethylbenzophenone. The Grignard reagent

from 62 grams (0.35 mole) of o-methylbromobenzene was prepared by the previously described method and added over a period of thirty minutes to a solution of 51 grams (0.33 mole) of o-methylbenzoyl chloride in 150 ml. of sodium-dried ether. The reaction was carried out in a 1-liter three-necked flask fitted with a magnetic stirrer, dropping funnel, and condenser with provision for maintaining a nitrogen atmosphere over the reaction mixture. After standing overnight the reaction mixture was poured onto 300 grams of crushed ice to which had been added 50 ml. of concentrated hydrochloric acid. The ether layer was separated and washed with two 150-ml. portions of a 5 per cent sodium hydroxide solution and with two 150-ml. portions of water. After drying the solution over anhydrous magnesium sulfate the solvent was evaporated. The product was distilled from the apparatus used to purify the esters. The fraction boiling at 176-180° C at 13mm. was collected. On standing the product solidified and was recrystallized from petroleum ether (b.p. 40-60° C). The melting point of the o,o'-dimethylbenzophenone was 67.5-70° C, and it was obtained in a 69 per cent yield.

Preparation of o,o'-diethylbenzophenone. The same procedure as above was employed, and a 62 per cent yield of product was produced from 34 grams (0.2 moles) of o-ethylbenzoyl chloride. The boiling point was 115-116° C at 0.2mm.

C. Reaction of Alkylphenyllithium Compounds with Esters and Ketones

Discussion of procedure

The alkylphenyllithium compounds were prepared from the corresponding o-alkylbromobenzenes and lithium metal in sodium-dried ether (50). The solutions were analyzed by titrating a filtered sample of

the reaction mixture with a standard hydrochloric acid solution. This method gave total alkalinity, but a blank determination showed no residual basicity in the ether, and Swain (36) reported that with proper care ether solutions of phenyllithium and o-methylphenyllithium exhibited negligible decomposition or reaction with ether, even after several months of storage. In this work at no time were the solutions of lithium reagent allowed to stand at 25° C for more than three hours, and analyses were performed before each series of runs.

The volume of solution calculated to contain 0.02 mole of the lithium reagent was diluted to 25 ml. with dry ether and allowed to react with 100 ml. of a solution containing 0.02 mole of the ester or ketone in dry ether. The reactions were carried out at 25° C. After one hour the reaction was quenched by the addition of a dilute hydrochloric acid solution, and the reaction mixture washed free of any phenolic material and dilute base.

The ether was replaced by toluene in a distillation which also served to azeotropically dry the products. The resulting solutions were then diluted to a known volume with Reagent Grade sodium-dried toluene. These solutions were analyzed by infrared spectrophotometry for tertiary alcohol, ketone, and unreacted ester.

This analytical method had previously been employed and checked by Pastor (51) and McComb (52). In a study similar to this one, but employing Grignard reagents, the spectrophotometrically determined yields were checked by derivatization of the alcohols, oxime formation of the ketones, and titration of the hydrolysis products of the unreacted esters.

Standardized procedures and reaction conditions were employed

throughout, and a typical reaction is given below.

Reaction of o-methylphenyllithium with phenyl o-methylbenzoate

To 75 ml. of sodium-dried ether in a 250-ml. three-necked flask was added 2.8 grams (0.4 gram atom) of lithium metal. The lithium was introduced by cutting a weighed length of lithium ribbon into small pieces with a scissors and allowing them to fall directly into the ether. The flask was fitted with a magnetic stirrer, dropping funnel, and condenser with a provision for maintaining an atmosphere of dry nitrogen over the reaction mixture at all times. To this was added 34.2 grams (0.2 mole) of o-methylbromobenzene dissolved in 75 ml. of dry ether over a period of thirty minutes. After the reaction began the temperature was kept under 30° C by means of a cold water bath. When the addition was complete the reaction mixture was stirred for thirty minutes at 25° C. The resulting suspension was allowed to settle and the liquid siphoned under nitrogen pressure through a three-inch pad of glass wool into a 250-ml. screw-cap bottle which had been flushed with nitrogen. The solution was then diluted with dry ether to an approximate 200 ml. mark made on the bottle. A 3-ml. sample was pipetted into 25 ml. of water and titrated to a phenolphthalein end point with a 0.1583N solution of hydrochloric acid. The volume of solution which contained 0.02 mole of o-methylphenyllithium was calculated from the following equation:

$$\frac{0.0200 \text{ mole} \times 3.00 \text{ ml.} \times 1000 \text{ ml./l.}}{17.12 \text{ ml. acid} \times 0.1538 \text{ mole/l.}} = 22.8 \text{ ml.}$$

A 100-ml. portion of a solution of 4.245 grams (0.200 mole) of phenyl o-methylbenzoate in dry ether was added to a 250-ml. three-necked

flask which had been swept with dry nitrogen for fifteen minutes. The flask was equipped with a magnetic stirrer, small dropping funnel, and condenser fitted for keeping an atmosphere of dry nitrogen over the system. The calculated volume of o-methylphenyllithium solution was diluted to 25 ml. with dry ether and added through the dropping funnel over a period of two minutes. After reacting for one hour at 25° C, the reaction was quenched by the addition of 50 ml. of a 5 per cent hydrochloric acid solution. The contents of the flask were transferred to a 250-ml. separatory funnel and the flask rinsed with small portions of water and ether. The aqueous layer was separated and the ether layer washed with three 50-ml. portions of a 3 per cent potassium hydroxide solution and two 50-ml. portions of distilled water. The ether solution was poured into a 300-ml. flask along with a few small ether rinsings of the funnel. The ether was distilled with the aid of a Dean-Stark condensation trap. When the volume of the residue reached approximately 25-35 ml., 200 ml. of Reagent Grade toluene was added and the distillation continued. When about 50 ml. of the solution remained the heat was removed and the residue allowed to cool. During this operation it was protected from moisture by a six-inch calcium chloride drying tube. The solution was then diluted with Reagent Grade sodium-dried toluene to 250 ml. in a volumetric flask. Infrared analysis showed a 35.3 per cent yield to tertiary alcohol, a 29.6 per cent yield of ketone, and 52.2 per cent unreacted ester.

D. Method of Analysis

The yields of alcohols and ketones and the amounts of unreacted ester were determined by infrared spectrophotometry using a Perkin-Elmer

Double Beam Spectrophotometer equipped with a calcium fluoride prism. All control settings were identical throughout. The same sodium chloride cells were used in their respective sample and reference positions in the instrument for each analysis.

Three standards were employed to determine each series of compounds. Benzophenone, absorbing at 6.00 microns served for the ketones, triphenylcarbinol, absorbing at 2.80 microns was used for the alcohols, and phenyl benzoate, absorbing at 5.75 microns was employed for the determination of unreacted ester. The justification for using one member of a series as an analytical standard has been discussed by Bellamy (53). Standard solutions of these compounds in toluene were made up and a calibration curve prepared for each series by plotting concentration versus transmittance. These curves were then employed to determine the yields of products for each of the reactions studied.

To determine if there was any interference among the alcohols, ketones, and esters in the infrared analyses, a known solution was made up containing 0.0200 moles per liter of triphenylcarbinol, benzophenone, and phenyl benzoate. This solution was then analyzed employing the prepared calibration curves. The concentrations found were 0.0203 moles per liter of alcohol, 0.0202 moles per liter of ketone, and 0.0195 moles per liter of ester. These results compare favorably with the expected accuracy of infrared analysis.

In some instances the transmittance of a product fell outside the range of the concentration curve, and in these cases the analyses were performed on diluted samples.

The infrared curves for a representative series of reactions are presented in Appendix I.

Determination of alcohols

Seven solutions of triphenylcarbinol (recrystallized, m.p. 162-162.5° C) in sodium-dried toluene (Reagent Grade) were prepared in the following concentrations: 0.0500, 0.0250, 0.0200, 0.015, 0.0100, 0.0050, and 0.0025 moles per liter. Both the reference and sample sodium chloride solution cells of 0.05 cm. thickness were filled with the solvent, and the 0 per cent and 100 per cent curves determined. Each of the solutions was then run and the transmittance found by dividing the distances between the peak height at 2.80 microns and 0 per cent transmittance by the distance between 0 and 100 per cent transmittance. Plotting concentration versus transmittance gave the curve presented in Figure 1.

Determination of ketones

Nine standard solutions of benzophenone (m.p. 47.5-48° C) in toluene were made up. The concentrations were: 0.0500, 0.0300, 0.0250, 0.0200, 0.0150, 0.0100, 0.0050, 0.0025, and 0.0015 moles per liter. The same procedure as above was used to prepare the calibration curve presented in Figure 2. Absorption occured at 6.00 microns.

Determination of unreacted esters

Figure 3 shows the calibration curve obtained at 5.75 microns for nine toluene solutions of phenyl benzoate (m.p. 70.5-71° C) in concentrations equal to those employed in the determination of ketones.

E. Isolation of Products

A number of tertiary alcohols and ketones were isolated from the reaction mixtures. The alcohols obtained from the ester reactions were compared by infrared spectra and mixed melting points with the corresponding alcohols obtained from the reactions of the appropriate phenyllithium compounds with ketones.

Figure 1. Infrared Calibration curve for Triphenylcarbinol

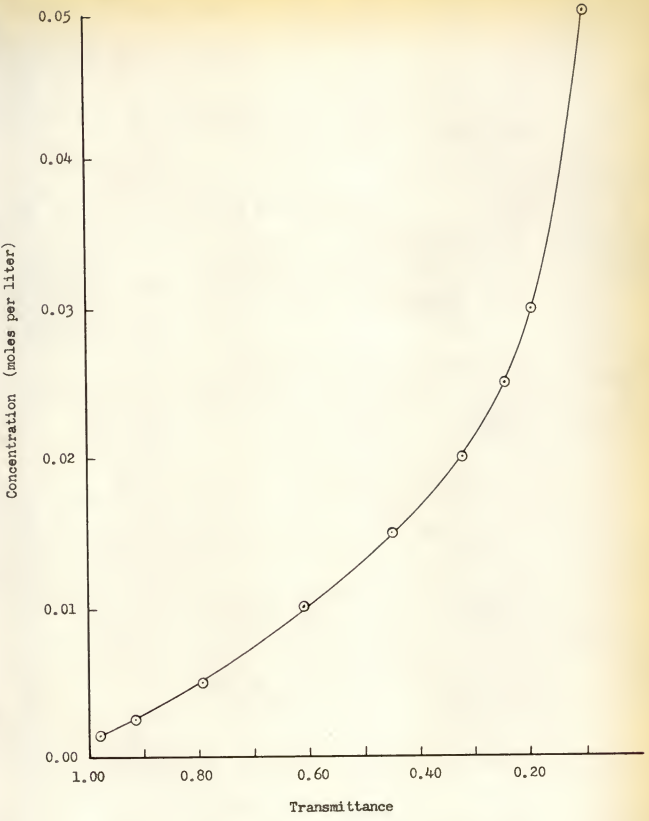


Figure 2. Infrared Calibration Curve for Benzophenone

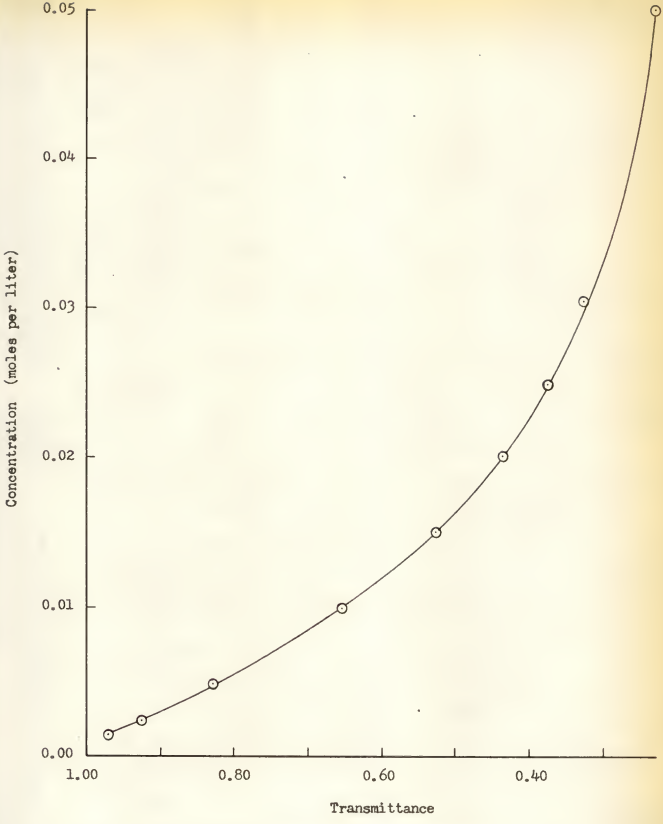


Figure 3. Infrared Calibration Curve for Phenyl Benzoate

After analyses, the toluene solutions from the reactions of a phenyllithium compound with a phenyl and o-cresyl benzoate were combined and the solvent removed by distillation. The residue was refluxed with 150 ml. of a 10 per cent potassium hydroxide solution to hydrolyze the ester. This mixture was then extracted with 300 ml. of the removed solvent in three equal portions. The toluene was again removed by distillation and the residue, on standing from periods of one day to one month, deposited a solid. In the reactions involving mesityl esters, this solid was the expected ketone. In the other reactions it was the tertiary alcohol.

In the reactions of the phenyllithium compounds with ketones, no ester was present and the hydrolysis was not needed. The alcohols were deposited after concentration of the reaction mixtures.

The products isolated are listed below with their observed melting points and the literature values, or in the case of unreported compounds, their analyses. They were recrystallized from petroleum ether (b.p. 40-60° C) to a constant melting point.

Triphenylcarbinol

Triphenylcarbinol was isolated from the reactions of phenyllithium with phenyl and o-cresyl benzoate and benzophenone. Both samples after recrystallization from petroleum ether had a melting point of 161-162° C. The mixed melting point was 160.5-162° C. The literature value is 162.5° C (54).

Diphenyl-o-methylphenylcarbinol

This alcohol was obtained from the reaction of phenyllithium with phenyl and o-cresyl o-methylbenzoate and the reaction of o-methylphenyllithium with benzophenone. The sample from the ester synthesis melted

at 98–99° C, and that from the ketone, 99–100° C. The mixed melting point was 98–99° C; the literature value is 98–99° C (55).

Diphenyl-o-ethylphenylcarbinol

The literature value for this alcohol is 77–78° C (46). The sample from phenyllithium and phenyl and o-cresyl o-ethyl benzoate melted at 79.5–80° C. The sample from benzophenone and o-ethylphenyllithium had the same range, as did the mixed melting point.

Di-o-methylphenylphenylcarbinol

The product from o-methylphenyllithium and phenyl and o-cresyl benzoate melted at 81–82° C. That from phenyllithium and o,o'-dimethylbenzophenone melted at 81.5–82° C. The mixed melting point was 81–82° C; the literature value is 82–83° C (55).

Tri-o-methylphenylcarbinol

This alcohol was obtained from o-methylphenyllithium and the o-methylbenzoates and from this lithium reagent and o,o'-dimethylbenzophenone. The literature melting point is 105° C (57). The melting point of both samples as well as the mixed melting point was observed to be 104.5–105° C.

Di-o-ethylphenylphenylcarbinol

The reaction of o-ethylphenyllithium and phenyl and o-cresyl benzoate and the reaction of phenyllithium with o,o'-diethylbenzophenone yielded this product. The melting point of the product from the first reaction was 73.5–74.5° C; that from the second was 73–74° C. The mixed melting point was 73–74° C.

Anal. Calcd. for $C_{23}H_{24}O$: C, 87.30; H, 7.64. Found: C, 87.28; H, 7.58.

Di-o-ethylphenyl-o-methylphenylcarbinol

The product from the reaction of o-ethylphenyllithium with phenyl and o-cresyl o-methylbenzoate melted at 92.5-93.5° C, while that from o-methylphenyllithium and o,o'-diethylbenzophenone melted at 93-94° C. The mixed melting point was 93-94° C.

Anal. Calcd. for $C_{24}H_{26}O$: C, 87.23; H, 7.93. Found: C, 87.39; H, 7.82.

Tri-o-ethylphenylcarbinol

This alcohol was obtained from the reactions of o-ethylphenyllithium with the o-ethylbenzoates and with o,o'-diethylbenzophenone. Its reported melting point is 101.5° C (58). The product from the ester reaction melted at 102-103° C, as did the product from the ketone reaction. The mixed melting point was also 102-103° C.

Diphenyl-o-isopropylphenylcarbinol

This product was obtained only from the reaction of o-isopropyllithium with benzophenone. The melting point was found to be 116-117° C.

Anal. Calcd. for $C_{22}H_{22}O$: C, 87.37; H, 7.33. Found: C, 87.17; H, 7.36.

Mesityl o-methylphenyl ketone

This ketone was isolated from the reaction of o-methylphenyllithium with phenyl and o-cresyl mesitoate. The melting point was 110.5-111° C; the literature value is 111° C (59).

Mesityl o-ethylphenyl ketone

The reaction of o-ethylphenyllithium with phenyl and o-cresyl mesitoate gave this product. The melting point was 82-83° C.

Anal. Calcd. for $C_{18}H_{20}O$: C, 85.67; H, 7.99. Found: C, 85.51; H, 8.02.

Chapter III

RESULTS AND DISCUSSION

A. Qualitative Correlations

The yields of alcohols and ketones obtained in the reactions of the phenyllithium compounds with the phenyl and o-cresyl benzoates are presented in Table 9. The yields of alcohols were found to be considerable in each instance even though the reactants were originally present in a 1:1 mole ratio. This is undoubtedly due to the relatively high reactivity of the organolithium compounds.

The maximum yields of alcohols were obtained in the reactions involving the nonhindered compounds as was expected. The introduction of an o-alkyl substituent in the phenyllithium reagent caused a marked decrease in the amount of alcohol formed. This effect was most noticeable when the substituent was changed from hydrogen to methyl; the yield was reduced from 80 to 58 per cent when phenyllithium and o-methylphenyllithium were reacted with phenyl benzoate. A further increase in the size of the substituent also decreased the yield of alcohol but to a lesser extent.

As the steric hindrance in the acyl portion of the ester was increased a similar decrease in the yield of alcohol was observed. However, these differences were much less than those observed when the hindrance in the phenyllithium reagent was increased. For example, the yield of alcohol was reduced only 15 per cent when phenyllithium

TABLE 9

PER CENT YIELDS OF ALCOHOLS AND KETONES IN REACTIONS OF PHENYLLITHIUM COMPOUNDS WITH ARYL ESTERS OF SUBSTITUTED BENZOIC ACIDS

Phenyllithium Compound	Substituted Benzoates: phenyl ester	o-cresyl ester			
	o-Hydrogen-	o-Methyl-	o-Ethyl-	Mesityl	p-Methyl-
A. Yields of Alcohols[a] (per cent)					
o-Hydrogen	80.3	72.0	65.1	33.9	82.0
	97.6	84.8	76.3	39.4	94.7
o-Methyl-	57.8	35.3	26.0	20.4	58.1
	72.2	49.3	33.7	24.8	76.3
o-Ethyl-	45.0	23.8	20.4	15.7	42.7
	54.6	36.2	28.4	22.0	59.7
o-Isopropyl-	28.0	19.6	18.1	14.9	34.8
	37.0	30.4	24.1	20.1	35.3
B. Yields of Ketones[a] (per cent)					
o-Hydrogen-	5.3	8.8	13.3	19.7	8.3
	1.2	4.9	10.8	14.3	1.8
o-Methyl-	17.1	29.6	36.1	21.8	21.3
	9.8	25.3	28.2	12.6	7.9
o-Ethyl-	24.8	39.9	38.2	21.9	29.6
	22.8	31.0	33.7	18.3	17.8
o-Isopropyl-	38.1	42.3	40.8	25.4	34.3
	29.6	39.7	35.9	17.1	26.8

a. Based on starting amount of phenyllithium compound.

was reacted with phenyl benzoate and phenyl o-ethylbenzoate, while a 52 per cent difference was observed when phenyllithium and o-isopropylphenyllithium were reacted with phenyl benzoate. These and the above effects can be explained by the fact that it takes two moles of the lithium compound to form the alcohol. Consequently the size of the substituents in this reagent would be expected to exert the most pronounced effect on the formation of the alcohol. Only when two o-substituents were present in the acyl portion of the ester, as in phenyl mesitoate, were steric effects in the ester as important as those in the lithium reagents.

When there was substantial hindrance present in both the ester and lithium reagent the differences in the yields of alcohols tended to disappear. This was evidenced in the reactions of o-ethyl- and o-isopropylphenyllithium with phenyl o-methylbenzoate and phenyl o-ethylbenzoate.

Finally, the yields of alcohols were consistently higher for the series of o-cresyl esters than for phenyl esters. This strongly suggests that the aroxy portion of the ester somehow influences the formation of the alcohol, and this effect will be discussed in greater detail in a later section.

The trend toward minumum yields of ketones undoubtedly caused by the ease of alcohol formation in the nonhindered reactions, was apparent in the low yields of ketones obtained in the reactions of phenyllithium with the esters. In a similar manner the lower yields of ketones from the o-cresyl esters compared to the phenyl esters can be explained by an increase in alcohol formation. A trend toward higher yields of ketones was observed when increased hindrance inhibited alcohol formation.

In attempting to evaluate the interplay of steric factors the raw yields of alcohols and ketones may be misleading. A low yield of ketone may reflect either a high reactivity of the system which results in an appreciable amount of alcohol being formed, or it may be the result of steric hindrance causing the system to be less reactive. A more meaningful representation of the results is given in Table 10. In this table the data are presented on the basis of the per cent ester reacting, calculated from the amount of ester consumed in the formation of both alcohol and ketone, and the per cent ester reacting which was converted to alcohol.

The per cent ester reacting was observed to be fairly constant throughout with the exception of the mesityl esters whose reactivity was 10–15 per cent lower than the average. Again this reflects the high reactivity of organolithium reagents with carbonyl compounds except in highly hindered systems. From these data it is evident that the differences in yields of alcohols and ketones were not due to differences in the reactivity of the system, but were the result of the steric effects of the o-substituents.

Although the reactivity of the mesityl esters was considerably lower, it was relatively independent of the steric effects in the attacking substituted phenyllithium compounds.

The p-methylbenzoates were employed to study the effects of an electron donating alkyl group which provides no steric inhibition to the reaction. Since in their reactions with the phenyllithium reagents their overall reactivity was approximately equal to that of the unsubstituted benzoates, the reactions studied can be considered relatively insensitive to the electronic effects of alkyl substituents in the acyl portion of the esters.

TABLE 10

PER CENT ESTER REACTING AND PER CENT ESTER REACTING CONVERTED TO ALCOHOL

Phenyllithium Compound	Substituted Benzoates: phenyl ester		o-cresyl ester		
	o-Hydrogen-	o-Methyl	o-Ethyl-	Mesityl	p-Methyl-
A. Amount of Ester Reacting[a] (per cent)					
o-Hydrogen-	45.4	44.8	45.8	36.6	49.3
	49.0	47.3	48.9	33.9	49.0
o-Methyl-	46.0	47.3	49.2	32.0	50.0
	45.9	49.9	45.0	25.0	46.0
o-Ethyl-	47.3	52.0	48.5	29.8	51.0
	50.1	50.0	47.9	29.8	47.7
o-Isopropyl-	52.0	52.2	47.8	32.8	51.5
	48.2	55.0	47.9	27.2	43.6
B. Amount of Ester Reacting Converted to Alcohol					
o-Hydrogen-	88.4	80.4	71.1	46.3	83.2
	97.4	89.7	78.0	58.1	96.6
o-Methyl-	62.8	37.4	26.4	31.9	58.1
	78.6	49.4	37.4	49.6	82.9
o-Ethyl-	47.6	22.9	21.0	26.3	41.9
	54.6	36.2	29.6	37.6	62.5
o-Isopropyl-	26.9	18.8	18.9	22.7	33.8
	38.4	27.6	25.2	36.8	40.5

a. Based on starting amount of ester.

The per cent ester reacting, or stated in another manner, the ratio of the number of moles of alcohol formed to the number of moles of ester consumed, again reflects the fact that two moles of lithium reagent participate in the production of the alcohol This is evidenced by the greater differences in the ratios present in the vertical series compared with the horizontal series.

When considering the horizontal relationships where steric factors in the lithium reagents remain constant and those in the acyl portion of the ester are varied from o-hydrogen to o-ethyl two trends are noticed. First, in the case of the nonhindered phenyllithium the decrease in the ratios are steady but slight. Secondly, in the case of the o-alkylphenyllithium compounds there is a sharp drop in their ratios when comparing their reactions with phenyl benzoate and phenyl o-methylbenzoate. These differences then become much less when comparing their reactions with phenyl o-methylbenzoate and phenyl o-ethylbenzoate, and with o-isopropylphenyllithium the ratios are the same.

These ratios also appear to be slightly higher for the mesityl esters than for the o-ethylbenzoates in their reactions with the o-alkylphenyllithium reagents. There is however a sharp decrease at this point in their reactions with phenyllithium.

The vertical relationships in the block pattern parallel the trends of the horizontal series, only the differences are more pronounced. In the first series, the reactions of the nonhindered phenyl benzoate, there is a steady decline in the ratios. In the reactions of the o-methyl- and o-ethylbenzoates there is a marked decrease when comparing their reactions with phenyllithium and o-methylphenyllithium. This decrease then becomes less apparent as steric effects in the

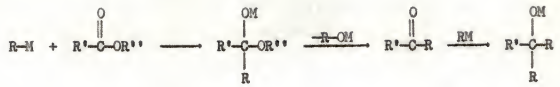
lithium reagent are increased. The mesityl esters also conformed to this vertical trend.

Diagonal values extending from right to left may also be considered. The two values, 71.1 and 47.6, illustrate the interaction between an o-hydrogen and an o-ethyl group and exemplify their characteristic effects when present in the ester or in the lithium reagent. In a similar manner the interaction between an o-hydrogen and an o-methyl group can be shown. Where o-substituents were present in both the ester and lithium compound very little difference was observed in these ratios. For example, the ratio was 26.4 for the reaction of o-methylphenyllithium with phenyl o-ethylbenzoate and was 22.9 for the reaction of o-ethylphenyllithium with phenyl o-methylbenzoate.

The trends observed with the o-cresyl esters were similar to those of the phenyl esters but with slightly higher ratios. The only effect of substituting o-cresyl for phenyl in the esters was to increase the yield of alcohol.

B. Mechanistic Evidence

One unanswered question concerning the reaction of esters with organometallic compounds is the manner in which the alcohol is formed. The following two reaction paths have been proposed (60, 61).



While it is generally agreed that the first step involves the reaction of the organometallic reagent with the ester, there is considerable controversy over the path of the second step. The basic question appears to be: Does the organometallic react with the ketone formed by the decomposition of the intermediate complex or directly with the complex itself? In this section the data from this work will be examined in the light of the above mechanisms with the hope of answering not only the questions posed but also some others related to organometallic reactions.

The experimental conditions employed in this study were chosen so as to minimize alcohol formation. But since the yields of alcohols were found to be appreciable in all reactions the second step in the reaction sequence must be faster than the first step. If this were not the case the yields of ketones would have been considerably higher, as the first step leads to this product. The alcohol yields however were not high enough to conclude that the second step is very rapid. Also, an examination of Table 10-A reveals that in most instances at the end of the reaction excess lithium reagent was present which could have participated in a very rapid second step. This unreacted lithium reagent in the presence of a large excess of ester also suggests a slow first step.

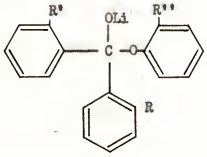
The sensitivity of the first step to steric factors can be seen as well from Table 10-A. Here the per cent ester reacting was found

to be relatively constant regardless of the steric factors present in the reagents employed. The only exceptions were the highly hindered mesityl esters.

It therefore seems reasonable to conclude that the first step in the process is a slow step and relatively independent of steric factors.

The sensitivity of step two to steric factors can be grasped from an examination of Table 10-B where the per cent ester reacting converted to alcohol is recorded in the block pattern. These data vary widely from the nonhindered and slightly hindered systems where 90 per cent of the reacting ester was converted to alcohol to the more highly hindered systems where only 20 per cent ended up as alcohol. It is apparent then that the second step is considerably more sensitive to steric factors than is step one.

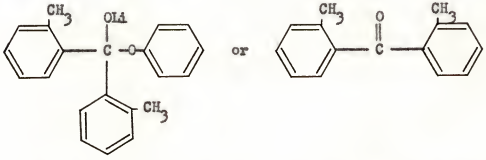
The second step in either of the aforementioned reaction schemes involves the reaction of the complex which, in this work, may be represented as



In the first of the suggested paths this complex reacts directly with the lithium reagent. In the alternate path the complex first decomposes to the ketone which them undergoes further reaction to form the alcohol.

Some indication of the preferred path can be obtained by comparing the yields of alcohols from the reactions of lithium compounds and hindered ketones with the appropriate data from Table 10-B. The phenyllithium compounds were reacted with a series of di-o-substituted benzophenones, and the results are listed in Table 11. It is clear from these data that there was only moderate steric interference to this reaction. These results are then compared with those from the ester reaction in Table 12.

According to the reaction paths the intermediates through which the alcohol is formed in the ester reactions would either be complex or the ketone. In the second example in Table 12 the intermediate would be either of the following:



If the second step involved a rapid decomposition of the complex followed by a reaction of the resulting ketone with the lithium reagent the differences in yields of alcohols should not be as great as those observed. In other words, the reactivity of o-methylphenyllithium towards o,o'-dimethylbenzophenone should be the same in either case. The table shows that the alcohol was produced in an 85 per cent yield in the reaction of this lithium reagent with the ketone, while in the reaction with phenyl o-methylbenzoate the conversion of the ester to alcohol was only 37 per cent. These differences are noted in each

TABLE 11

PER CENT YIELDS OF ALCOHOLS FROM REACTIONS OF PHENYLLITHIUM COMPOUNDS WITH SUBSTITUTED BENZOPHENONES

Phenyllithium Compound	Benzophenone	Benzophenones o,o'-Dimethyl-	o,o'-Diethyl-
o-Hydrogen-	97.6	93.2	85.8
o-Methyl-	91.8	85.3	77.0
o-Ethyl-	88.4	82.9	68.1
o-Isopropyl-	86.8	76.4	64.2

TABLE 12

COMPARISON OF YIELDS OF ALCOHOLS FROM SUBSTITUTED BENZOPHENONES AND ESTER INTERMEDIATES

Phenyllithium Compound	Yield of Alcohol (per cent)			Yield of Alcohol (per cent)		
	Substituted Benzophenones			Ester Intermediates		
	o,o'-Di-H	o,o'-Di-CH_3	o,o'-Di-C_2H_5	o,o'-Di-H	o,o'-Di-CH_3	o,o'-Di-C_2H_5
o-Hydrogen-	97.6			88.4		
o-Methyl-		85.3			37.4	
o-Ethyl-			68.1			21.0

example. Since the lithium reagent reacted much more readily with the ketone than with the intermediate of the ester reaction, it is suggested that the intermediate is not the ketone in this case.

Further support for the notion that the rate of the second step is controlled by the complex formed in step one is apparent when the yields of alcohols from the series of reactions involving phenyl esters are compared with those from reactions involving o-cresyl esters. In all cases the o-cresyl esters gave higher yields of alcohols. If step two involves the reaction of the lithium reagent with a ketone as the rate determining process, the yields of alcohols should have been found independent of the phenolic portion of the ester.

This line of reasoning does not exclude the possibility of a slow decomposition of the complex to ketone as a rate determining step. However, a comparison of the reactions of the phenyllithium reagents with o- and p-cresyl esters, formulated in Table 13, shows that the yields of products are nearly identical in both cases, and that these yields are significantly greater than those from the reactions involving phenyl esters. These results are consistent only with the interpretation that the complex reacts directly with the lithium reagent. These results also indicate that the effect of this substituent in the phenol portion of the ester upon the yield of alcohol is electronic rather than steric.

If the o-methyl group acts sterically it should tend to loosen the complex and hasten its slow decomposition into ketone. Then a rapid reaction of this ketone with the lithium reagent would account for the higher yields of alcohols with the o-cresyl esters than with the phenyl esters. But the reactions of the p-cresyl esters should then have paralled those of the phenyl esters as their steric effects should be approximately the same.

TABLE 13

RESULTS FROM REACTIONS OF PHENYLLITHIUM COMPOUNDS WITH *p*-CRESYL ESTERS OF SUBSTITUTED BENZOIC ACIDS

Phenyllithium Compound	Yield of Alcohol[a] (per cent) — Ester		Yield of Ketone[a] (per cent) — Ester	
	o-Hydrogen	*o*-Methyl	*o*-Hydrogen	*o*-Methyl
o-Methyl-	71.5 (72.2)[c]	47.7 (49.3)	11.5 (9.8)	24.7 (25.3)
o-Ethyl-	56.1 (54.6)	34.3 (36.2)	21.1 (22.8)	31.9 (31.0)
	Amount of Ester Reacting[b] (per cent)		Amount of Ester Reacting Converted to Alcohol (per cent)	
o-Methyl-	47.2 (45.9)	48.5 (49.9)	75.8 (78.6)	49.2 (49.4)
o-Ethyl-	49.2 (50.1)	49.1 (50.0)	57.1 (54.6)	34.9 (36.2)

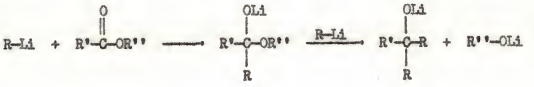
a. Based on starting amount of phenyllithium compound.

b. Based on starting amount of ester.

c. Yields from *o*-cresyl esters in parentheses.

If the o-methyl substituent exerts an electrical effect upon the decomposition of the complex, a decrease rather than increase in alcohol formation would have been observed, as the phenoxy moiety is a better leaving group than o-methylphenoxy when leaving with its electrons. If, on the other hand, the complex reacts directly with the lithium reagent the electron donating properties or the o-methyl substituent would increase the basicity of the oxygen atoms in the complex, thereby facilitating its further reaction. If this is the preferred path then both the o- and p-cresyl esters should give parallel results as their electrical properties are identical. Table 13 shows that this was the observation.

Thus the data reported herin are consistent with the following sequence for the reaction of organolithium reagents with esters.



C. Quantitative Treatment of the Data

One of the goals of this research has been to attempt to develop quantitative expressions which relate factors indicating the relative importance of steric hindrance to other factors indicating the relative size or hindering effect of the various substituents. While no attempt was made to obtain precise kinetic measurements the data from this work were used to develop expressions for the relative rate factors for the two steps of the proposed reaction path. The equation for the first step in the reaction sequence has been developed in Appendix II and is

given by

$$k_1' = k_1 \frac{\ln([E']_o/[E'])}{\ln([E]_o/[E])}$$

where k_1 is the rate factor for the reference reaction of phenyllithium with phenyl benzoate, and is given the value of 1, $[E]_o$ is the initial ester concentration, and [E] is the concentration of ester at the end of one hour in the reference reaction, while k_1', $[E']_o$ or [E'] are the corresponding values for the reaction under consideration. The calculated relative rate factors are listed in Table 14-A and can be seen to be relatively independent of steric factors present in any of the three steric areas. The only exceptions were found in the reactions of the mesityl esters where two o-positions in the acyl portion of the ester were substituted.

The following equation has been derived in Appendix III and gives the relative rate factors for the second step in the reaction sequence, i. e., the reaction between the complex and the phenyllithium reagent

$$\left[\frac{[K]}{[A]} + 1\right] \frac{[K]\ 0.342}{E_c} = \frac{k_1'}{k_2}$$

In this equation k_2 is the relative rate factor for step two, k_1' is the relative rate factor for the first step, [K] is the final concentration of the ketone, [A] is the final concentration of the alcohol, and E_c is the amount of ester consumed in moles per liter. These values of k_2 were calculated and are presented in Table 14-B. An examination of this table reveals that these values changed significantly with changing steric factors and points out the high sensitivity of the second step to steric effects.

TABLE 14

RELATIVE RATE FACTORS FOR THE PROPOSED STEPS IN THE REACTIONS OF PHENYLLITHIUM COMPOUNDS WITH ARYL ESTERS OF SUBSTITUTED BENZOIC ACIDS

Phenyllithium Compound	Substituted Benzoates: o-Hydrogen-	o-Methyl-	o-Ethyl-	phenyl ester / o-cresyl ester: Mesityl	p-Methyl-
A. Relative Rate Factors for the First Step (k_1')					
o-Hydrogen-	1.00	0.982	1.01	0.757	1.12
	1.11	1.06	1.11	0.682	1.11
o-Methyl-	1.02	1.06	1.12	0.638	1.15
	1.02	1.15	0.991	0.472	1.02
o-Ethyl-	1.06	1.21	1.10	0.592	1.16
	1.15	1.15	1.08	0.580	1.07
o-Isopropyl-	1.21	1.21	1.07	0.671	1.19
	1.09	1.32	1.08	0.533	0.945
B. Relative Rate Factors for the Second Step (k_2)					
o-Hydrogen-	22.3	11.8	7.27	1.89	16.2
	1.00	27.0	11.5	2.75	88.1
o-Methyl-	5.02	1.84	1.18	0.880	4.56
	11.0	3.27	1.71	1.35	1.45
o-Ethyl-	2.82	1.06	0.859	0.623	2.44
	4.02	2.00	1.34	1.02	5.27
o-Isopropyl-	1.29	0.818	0.656	0.569	1.76
	1.99	1.48	1.06	0.911	1.79

These relative rate factors can be employed in the same manner as rate constants to evaluate steric effects in organic reactions, although the results are expected to be less reliable than those obtained from the precise kinetic data available in simpler systems. However, the value of the treatment lies in the extent to which the results correlate the data and fit with other knowledge about the reaction.

Taft (63, 64) has developed and tested the linear steric energy relation

$$\ln \frac{k}{k_o} = \delta E_s$$

where k/k_o is the ratio of rate constants for two reactions of the same type differing only in steric factors; k_o is the rate constant for the reference reaction, δ is a measure of the susceptibility of the reaction to steric factors, and E_s is the steric substituent constant or a measure of the bulk of the substituent.

As an extension of the Taft equation it is proposed that the data of this work might be successfully to an equation of the form

$$\ln \frac{k}{k_o} = xE_m + yE_a + zE_p$$

where k/k_o is the ratio of rate factors using the unsubstituted benzene derivitives as the reference, x, y, and z, are constants which refer to the relative importance of steric effects in the organolithium reagent, the acyl portion of the ester, and the phenolic portion of the ester respectively, and E_m, E_a, and E_p are the steric substituent constants for the groups in the three steric areas.

An examination of Table 14 reveals that only the k_2 values – the relative rate factors for the process

can be fitted to this type of equation, as k_1 was found to be almost independent of steric effects. Consequently the equation may now be expressed as

$$\ln \frac{k}{k_o} = xE_m + y(Em + E_a) + zE_p$$

because the second step involves the reaction of the organometallic with the complex which was formed by a prior reaction of the lithium reagent with the ester.

Assuming electrical factors to be of secondary importance, assigning E values of 0.00 and -1.00 to the o-hydrogen and o-methyl substituents respectively, and employing standard data-fitting techniques, the best fit of the data from Table 14-B to this equation gives

$$\ln \frac{k}{k_o} = 0.86E_m + 0.70(E_m + E_a) + zE_p$$

The precision of this fit is within 20 per cent.

The values for z are not specified because they were found to be erratic and well beyond the limit found for x and y. This lack of correlation for z is consistent with the interpretation, previously justified, that the effect of the o-cresyl group is electrical rather than steric. The values of x and y are valid for the series of phenyl esters as the assumed value of E for o-hydrogen is 0.00 and the last term in the equation becomes zero.

From the first approximations of x and y the E values for the o-ethyl and o-isopropyl substituents were calculated to be -1.48 and -1.72 respectively. The equation was then transferred to the form

$$\frac{\ln(k/k_o)}{E_m} = x + y\,\frac{(E_m + E_a)}{E_m}$$

and using the above E values, a plot of $\ln(k/k_o)/E_m$ versus $(E_m + E_a)/E_m$ was made, thereby determining final approximations of x and y. This plot is presented in Figure 4.

Since the values of x and y were found to be 0.86 and 0.70 respectively, it appears that the second step in the reaction scheme, viewed broadly, is slightly more sensitive to steric effects in the organometallic than in the complex.

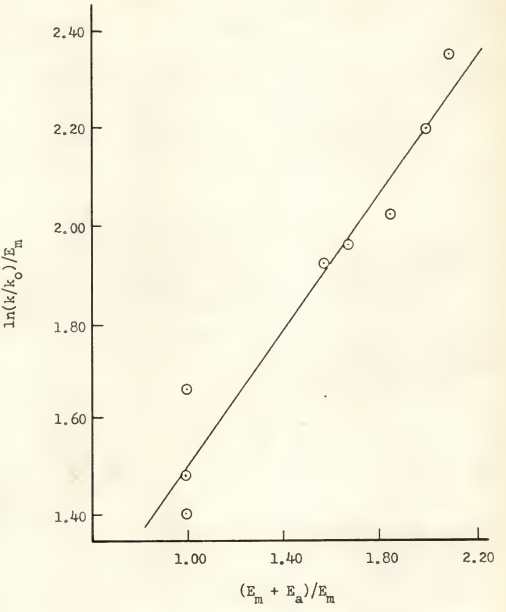


Figure 4. Plot of $\ln(k/k_o)/E_m$ versus $(E_m + E_a)/E_m$

Chapter IV

SUMMARY

In the course of this work the following new compounds were isolated and identified:

o-cresyl mesitoate

di-o-ethylphenylphenylcarbinol

di-o-ethylphenyl-o-methylphenylcarbinol

diphenyl-o-isopropylphenylcarbinol

mesityl o-ethylphenyl ketone

In the reactions of o-alkyl substituted phenyllithium compounds with phenyl and o-cresyl esters of alkyl substituted benzoic acids the formation of the initial complex was found not to be appreciably affected by steric factors of the order of magnitude employed in the study. The yields of tertiary alcohols obtained were shown to decrease in a consistent pattern as the steric effects of the substituents were increased. Substitution in the o-position of the lithium reagent caused the greatest hindrance to the alcohol formation.

The fact that in all cases the o-cresyl esters gave higher yields of alcohols than the corresponding phenyl esters suggested that the alcohol was formed by the reaction of the lithium reagent with the complex and not an intermediate ketone. By comparing the reactions of a series of p-cresyl esters with the o-cresyl esters this effect of increasing the yields of alcohols was shown to be electrical rather than steric.

Also, a study of the reactions of the lithium reagents with o,o'-disubstituted benzophenones further supported the notion of a direct reaction of the complex.

The two steps in the reaction path having been elucidated, expressions for relative rate factors were derived and the values for the resulting k_1' and k_2 calculated. The values for k_2 (k_1' was found to be independent of steric factors) were then employed to calculate steric susceptibilities and steric substituent constants in the linear steric energy relationship

$$\ln (k/k_o) = xE_m + y(Em + E_a) + zE_p$$

The best fit of the data to this equation gave values of 0.86 for x and 0.70 for y. Assigning E values of 0.00 to o-hydrogen and -1.00 to o-methyl, E values of -1.48 and 1.72 were calculated for o-ethyl and o-isopropyl respectively. The z susceptibility factor varied outside the limits set for x and y which is consistent with the interpretation that the substituents in the phenol portion of the ester employed in this work exerted an electrical effect upon the formation of alcohol.

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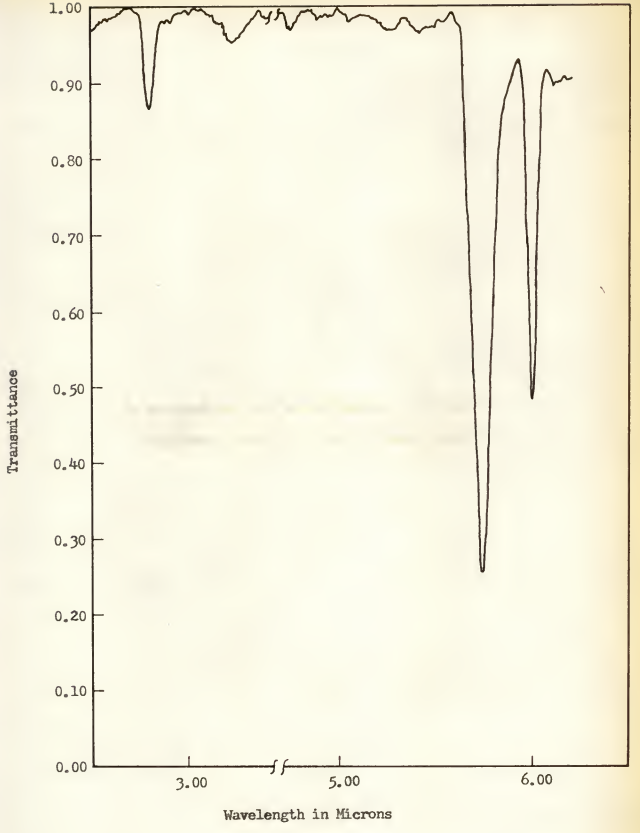
APPENDICES

APPENDIX I. INFRARED CURVES FOR THE REACTIONS OF *o*-METHYLPHENYLLITHIUM WITH A SERIES OF PHENYL AND *o*-CRESYL ESTERS OF SUBSTITUTED BENZOIC ACIDS

The following pages contain the infrared curves of the reaction mixtures obtained from the reactions of *o*-methylphenyllithium with the indicated esters.

Figure 5. Infrared Curve for the Reaction of o-Methylphenyllithium with Phenyl Benzoate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Transmittance
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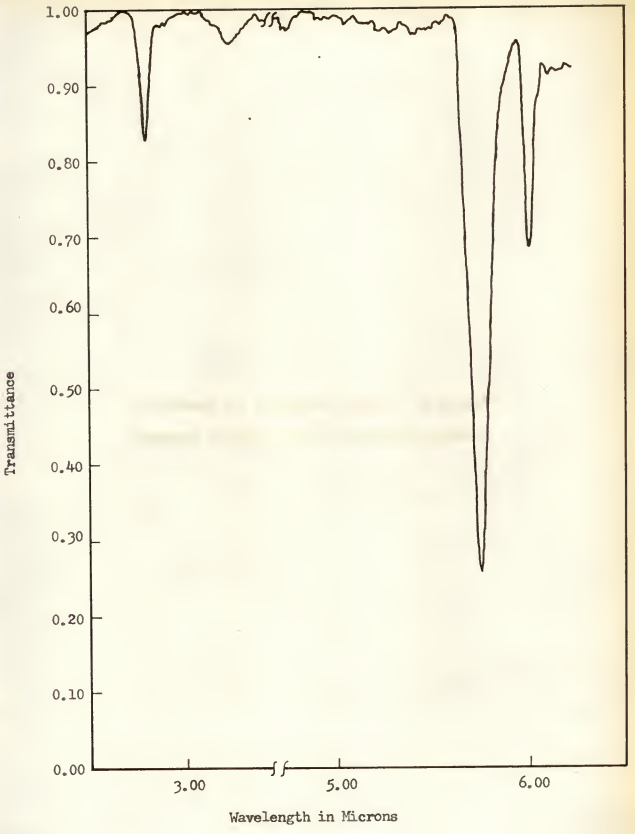
Wavelength in Microns

Figure 6. Infrared Curve for the Reaction of o-Methylphenyllithium with o-Cresyl Benzoate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Transmittance
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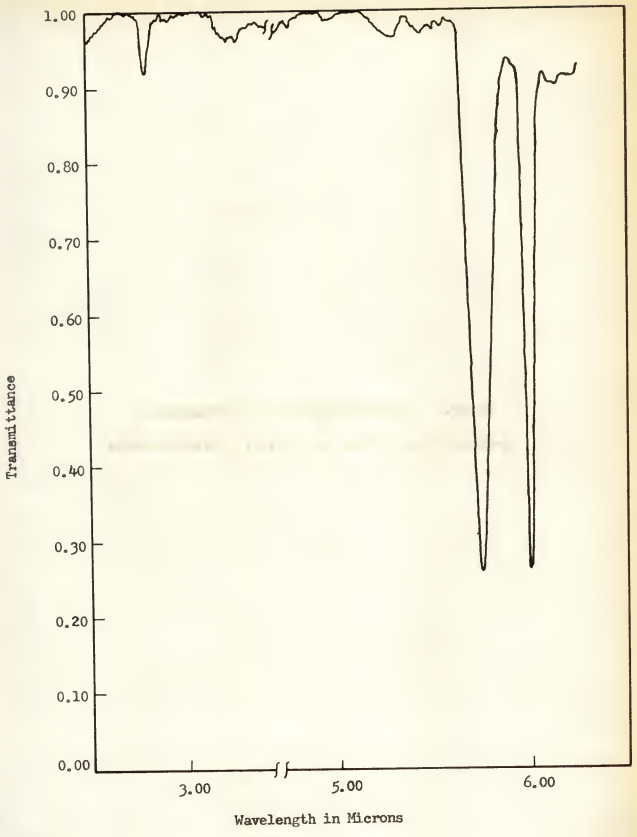
Wavelength in Microns

Figure 7. Infrared Curve for the Reaction of o-Methylphenyllithium with Phenyl o-Methylbenzoate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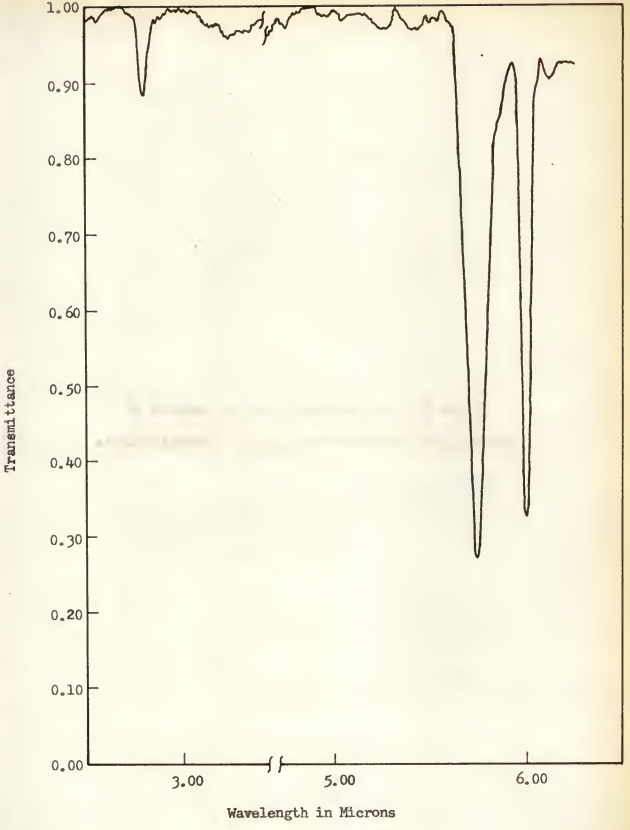
Wavelength in Microns

Figure 8. Infrared Curve for the Reaction of o-Methylphenyllithium with o-Cresyl o-Methylbenzoate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Wavelength in Microns

APPENDIX II. DERIVATION OF AN EXPRESSION FOR THE RELATIVE RATE FACTORS FOR THE FIRST STEP IN THE REACTION SEQUENCE

Consider the reaction of organolithium compounds with esters to be represented by

$$E + R\text{-}Li \xrightarrow{k_1} C$$

$$C + R\text{-}Li \xrightarrow{k_2} A + D$$

where E represents the ester, R-Li the organolithium reagent, C the complex, and A the alcohol.

The rate of disappearance of the ester is given by

$$-\frac{d[E]}{dt} = k_1[E][R\text{-}Li] \qquad \text{Eq. 1}$$

The concentration of lithium reagent at anytime is

$$[R\text{-}Li] = [R\text{-}Li]_o - [K] - 2[A] \qquad \text{Eq. 2}$$

where $[R\text{-}Li]_o$ is the initial concentration of the lithium reagent, [K] is the concentration of ketone or the concentration of the complex which when hydrolyzed would yield ketone, and [A] is the concentration of alcohol. Also, the amount of ester consumed in moles per liter is

$$E_c = [E]_o - [E] = [K] + [A] \qquad \text{Eq. 3}$$

Solving equation 3 for [K] and substituting this value into equation 2 gives

$$[R\text{-}Li] = [R\text{-}Li] - [E]_o + [E] - [A] \qquad \text{Eq. 4}$$

In all the reactions studied the initial concentrations of ester and lithium reagent were equal, so equation 4 becomes

$$[R\text{-}Li] = [E] - [A]$$

Substituting this value into equation 1 gives

$$-\frac{d[E]}{dt} = k_1[E]([E] - [A])$$

Dividing this equation by [E] and rearranging gives

$$-\frac{d\ln[E]}{dt} = k_1([E] - [A]) \qquad \text{Eq. 5}$$

Upon integration of equation 5 between the limits $[E] = [E]_o$ and $[E] = [E]_t$ and $t = 0$ and $t = t$ gives

$$\ln\frac{[E]_o}{[E]_t} = k_1\int_o^t([E] - [A])\,dt$$

This expression cannot be integrated because in this work the variation of [E] and [A] with time was not determined. However, the expression is valid for each of the reactions studied.

If the equations for two reactions in the series are compared the result is

$$\frac{\ln\frac{[E]_o}{[E]_t}}{\ln\frac{[E']_o}{[E']_t}} = \frac{k_1\int_o^t([E] - [A])\,dt}{k_1'\int_o^t([E'] - [A'])\,dt} \qquad \text{Eq. 6}$$

where the reference reaction is in the numerator and the reaction to which it is compared is in the denominator.

Assuming

$$\frac{\int_0^t ([E] - [A])\,dt}{\int_0^t ([E'] - [A'])\,dt} = 1$$

equation 6 becomes

$$k_1' = k_1 \frac{\ln([E']_o/[E']_t)}{\ln([E]_o/[E]_t)}$$

APPENDIX III. DERIVATION OF AN EXPRESSION FOR THE RELATIVE RATE FACTORS FOR THE SECOND STEP OF THE REACTION SEQUENCE

Again consider the reaction scheme

$$E + R\text{-}Li \xrightarrow{k_1} C$$

$$C + R\text{-}Li \xrightarrow{k_2} A + D$$

Then

$$\frac{d[C]}{dt} = k_1[R\text{-}Li][E] - k_2[R\text{-}Li][C] \qquad \text{Eq. 1}$$

In most treatments of consecutive reactions this equation can be set equal to zero with the assumption that C is a reactive intermediate which reacts rapidly, and whose concentration never changes significantly during the course of the reaction. Evidence from this study indicates that C does not react rapidly and is hydrolyzed to ketone at the end of the reaction.

As an alternate to the steady state procedure the following scheme is suggested. From the above reaction sequence the rate of formation of alcohol is given by

$$\frac{d[A]}{dt} = k_2[R\text{-}Li][C] \qquad \text{Eq. 2}$$

Dividing equation 1 by equation 2 results in

$$\frac{\frac{d[C]}{dt}}{\frac{d[A]}{dt}} = \frac{k_1[E]}{k_2[C]} - 1 \qquad \text{Eq. 3}$$

Integration of this equation between the limits $[C] = [C]_o = 0$ and $[C] = [C]_t$, $[A] = [A]_o = 0$ and $[A] = [A]_t$, and $t = 0$ and $t = t$ gives

$$\frac{[C]_t}{[A]_t} = \frac{k_1 \int_o^t [E]\,dt}{k_2 \int_o^t [C]\,dt} - 1 \qquad \text{Eq. 4}$$

Now the following integrals must be considered.

$$\int_o^t [E]\,dt \quad \text{and} \quad \int_o^t [C]\,dt$$

To evaluate $\int_o^t [E]\,dt$ it is assumed that

$$[E] = [E]_o e^{-\alpha t} \qquad \text{Eq. 5}$$

Then

$$\int_o^t [E]\,dt = \int_o^t [E]_o e^{-\alpha t} = -\frac{[E]_o(e^{-\alpha t} - 1)}{\alpha}$$

Since the numerator of this result can be expressed as $[E]_o - [E]_o e^{-\alpha t}$ which is an expression for the amount of ester consumed in the reaction, the value of the integral can be expressed as

$$\int_0^t [E]\,dt = \frac{E_c}{\alpha}$$

where E_c is the amount of ester consumed in moles per liter.

Equation 5 can then be used to obtain values for α for each reaction since E_c was measured at the end of the reaction time of one hour. In order to generalize this expression a value of 1.93×10^{-4} was calculated from the observation that in most examples approximately 50 per cent of the ester was consumed.

To evaluate $\int_0^t [C]\,dt$ it was first assumed that

$$[C] = c^{\beta t} - 1$$

From this equation and the data β can be evaluated and the integral determined. However, the changes in [C] are so small that usual tables of logarithms do not give reliable values. A better approximation is to assume a value of $([C]\Delta t)/2$ for this integral.

Having evaluated these two integrals the values may then be substituted into equation 4 to give

$$\frac{[C]_t}{[A]_t} = \frac{k_1 E_c/\alpha}{k_2[C]\Delta t/2} - 1$$

Using the previously indicated value for α, the known reaction time of 3600 seconds, and realizing that $[C]_t = [K]_t$ this equation reduces to

$$\left[\frac{[K]_t}{[A]_t} + 1 \right] \frac{[K]_t \, 0.342}{E_o} = \frac{k_1}{k_2}$$

BIOGRAPHICAL SKETCH

Ronald Walter Von Allmen was born October 18, 1934, at Louisville, Kentucky. Upon graduating from du Pont Manual High School in June 1952, he attended Bellarmine College where he was awarded the degree of Bachelor of Arts in June 1956.

In September 1956, he entered Xavier University, Cincinnati, Ohio, where for two years he held a position as a graduate assistant in the Department of Chemistry. He received the Master of Science degree in August 1958.

Since September 1958, he has attended the University of Florida where he has held appointments as graduate assistant, teaching assistant, and interim instructor.

He is a member of Alpha Chi Sigma Chemical Fraternity and the American Chemical Society.

This dissertation was prepared under the direction of the chairman of the candidate's supervisory committee and has been approved by all members of that committee. It was submitted to the Dean of the College of Arts and Sciences and to the Graduate Council, and was approved as partial fulfillment of the requirements for the degree of Doctor of Philosophy.

December 22, 1962

Dean, College of Arts and Sciences

Dean, Graduate School

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